

IN THE SPECIFICATION:

As requested by the Examiner, incorrect paragraph reference number contained in the previous response and resubmitted response to the Office Action of April 14, 2004, are herewith corrected in the amendments presented again below. No other changes have been made to these amendments to the specification other than those indicated by the Examiner:

Please amend the following paragraphs as indicated.

[0078] In another embodiment, the leads can be comprised of an electrically conductive fluid. Depending upon the application, such a fluid can be electrically conductive, thermally conductive or both thermally and electrically conductive. With reference to FIGS. 4A and 4B, electrical connection to the functional component can be accomplished through the use of microchannel networks 204 filled with the conductive fluid 204 and in fluid connection with the component 206. The dimensions of the microchannels are in accordance with the required design parameters of the leads. One variation on this approach would be that in which the electrically conductive fluid comprises the functional component itself, for instance, a serpentine channel that is filled with an electrically conductive fluid is an example of a working design for a heater element. Another variation would be to introduce a conductive fluid into the microchannels which will subsequently cure into a solid form that is stable and integral to the device. In the alternative, localized regions of the fluid can be selectively cured, i.e., photocurable fluids selectively exposed to UV light. Such designs may be particularly useful for the manufacturing of the provided devices, especially those that may be multidimensional or multi level. Curable conductive fluids would include epoxy resins and inks comprising an electrically conductive portion, usually metal or graphite. Other examples of electrically conductive fluids include uncured inks and ionic or electronic liquid conductors. For example, aqueous salt solutions and liquid metals are useful in the invention. Conveniently, liquid metals such as mercury can be used in order to avoid hydrolysis and the generation of gases from reduction and oxidation processes present at electrodes where ionic solutions are utilized. Such reactions can also be minimized through the use of ionic entities in nonaqueous solvent such as methanol and the like.

[0095] FIG. 5 shows one design for an electrochemical detector that demonstrates such a configuration. The detector is comprised of interdigitated detection elements 501, leads 507 and contacts 513. The detection elements 501 are located near the end of the capillary channel 503 for purposes of optimizing detection signals. For a general description of electrochemical detectors and their placement relative to electrophoretic channels, see U.S. Patent No. 5,906,723 which is incorporated herein by reference. If the component is to serve as a driving electrode for controlling movement of fluids, the electrode should be placed in fluid connection with the channel 503, either directly or through a permeation layer, at opposite ends, alongside, or in localized regions of the channels. Preferably the electrode 509, connected through lead 511 to contact 513, is placed or positioned in a reservoir 505 located at the end of the channel 503. The driving electrode can be provided in a variety of shapes and dimensions, such as a half circle 509 or whole circle in fluid connection with the reservoir 505.

[0096] FIGS. 6A and 6B show another configuration of the present invention having integrated electrode heating elements. Referring to FIG. 6A, a partial top view of a device 450 is shown having an electrically conducting ink pattern incorporated therein. In particular, FIG. 6A depicts a heating element 454 as a single linear strip ink electrode. The ink pattern also includes leads 456 and contacts 458 to provide a convenient electrical connection to a voltage or current source. Current is applied to the heating element via contacts and leads to heat the channel 460. Also, the heating element 454 is not in direct contact with the channel and is separated by a cover 462. Cover 462 is shown bonded to substrate 464 thereby enclosing channels 460. The device 450 also may include a support-466. Notably, this configuration has been found to suitably heat materials in the channel 460. Further, the heat may be controlled by varying other properties or parameters of the device such as the voltage supplied to the electrode.

[0097] FIGS. 6C and 6D show another variation of the present invention comprising a heating element. In this configuration, electrically conducting ink heating element 470 is serpentine shaped and is shown having square-like turns. The pattern, however, need not be square-like and other patterns may be employed. The configuration shown in FIGS. 6C and 6D also include contacts 472 and leads 474. The heating element 470 is positioned below cover 476 and is not in fluid communication with channel 478. Cover 476 is shown bonded to substrate 480 thereby enclosing channel 478. Support 482 may also be included beneath heating element 470. Using this configuration, we have found that the measured resistance is higher than a

straight strip and that materials in channel 478 may be heated when voltage is applied to the electrically conducting ink pattern 470.

[0099] Another configuration is shown in FIG. 8 where the driving electrode 612, located in reservoir 608, is merely an extension of the lead, whereby hydrolysis is minimized by the smaller surface area of the provided electrode. For purposes of controlling temperature, the components can be configured as heaters placed within certain localized regions along the channel of interest, e.g. 604. One design for such a heater includes a serpentine-like heater element 602, leads 606, and contacts for the power supply 610. Another heater design includes a heater element that is a solid band as described in FIG. 6A above and variations or combinations in between.

[00100] With reference to FIG. 9, ~~a heater~~ heater 100 integrated on the surface of a norbornene based substrate is shown whereby the heating element portion 101 of the component is serpentine in shape and is of a length of about 230 mm. Its width is approximately 100 μm and its thickness is about 2000 Å. The heater is comprised of gold with a resistance of 790 Ω under an operating voltage of 25 V. The leads providing current to this heater are incorporated into the gold film, also having a thickness of about 2000 Å. Their width is also about 100 mm while their length is about 12 mm. The intended application of this particular heater design is to control the temperature in a microfluidic channel. Its general orientation is orthogonal to the particular length of a microchannel so as to heat the channel contents in a localized region of the device. Techniques for depositing metal films are described in U.S. Provisional Application 60/233,838 which, as mentioned above, is incorporated by reference in its entirety.

[00109] For DNA separation, the ink-integrated DNA chip has a separation length of 18.5 cm and an offset of 250 μm . The dimension of the channel was 50 by 120 μm . This device gave all the expected 18 DNA fragments, as shown in FIG. 12A. The crossover plot shows separation of up to 385 base pairs DNA molecules on an acrylic chip at room temperature, better than the results using Pt wire as electrodes (340 bp, FIG. 12B). However, as evidenced in FIGS. 12A and 12B respectively, the signal from the chip using carbon ink as electrodes is about 30% of that from chip using Pt as electrodes. The carbon ink on plastic chip can survive at least 10 runs, each run takes over 3000 s, suggesting that the printed carbon ink is very robust and reliable.

[00142] FIG. 18 shows device 800 with an integrated heater 810. In each this case a heater 810 was placed outside of the ~~microchannels~~ microchannels 815 as shown in FIG. 18, and a temperature sensor 820 was attached to the opposite side of device 800, across the substrate and channels from heater 810. The heating element 810 was thus not in fluid communication with the channels 815. Results for various heating elements are provided in FIGS. 19-21 (FIGS. 19A and 19B corresponding to metallic heaters and FIGS. 20A to 21C corresponding to ink heaters).

[00146] Cyclic testing was also carried out on various heating elements of the present invention. That is, voltage was increased and decreased periodically to determine cyclic performance of an electrically conducting ink electrode. FIG. 22 21C shows the thermal cycling for PCR using ink screen printed heaters on a plastic chip. A commercial heat strip was also tested for comparison purposes. Reference numerals 850 and 860 correspond to the ink and metal electrodes respectively. Both electrodes were raised to 95°C. for 45 s; 61°C. for 30 s; and 72°C. for 45 s. This data indicates the commercial metal heat strips and the electrically conducting ink electrodes of the present invention behave similarly.

[00148] Electrically conducting ink electrodes can also be used as a on-chip electrochemical detector as shown in FIGS. 22A and 22B. At least one electrode 870, connected via contact pad 880, may be positioned in the channel 874 and in contact with the subject sample. For example Cu₂O-doped carbon ink can be patterned on a cover 876 and used as working electrode to detect carbohydrate, amino-acid. The counter and reference electrodes can be also prepared on the chip.